UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,060	01/03/2002	Frank Frantzen	FRAN3006/REF	1169

23364 7590 04/03/2007

BACON & THOMAS, PLLC
625 SLATERS LANE
FOURTH FLOOR
ALEXANDRIA, VA 22314

EXAMINER	
FOSTER, CHRISTINE E	
ART UNIT	**PAPER NUMBER**
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/869,060	FRANTZEN, FRANK	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/14/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-57* is/are rejected.

7)☒ Claim(s) *24,26,35,36,38,44,45,52,53 and 57* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/14/2006 has been entered.

2. Claims 24-26, 30, 32, 35-44 were amended. New claims 45-57 have been added. Claims 24-57 are currently pending and under examination.

Rejections/Objections Withdrawn

3. The rejections of claims 24-43 under 35 USC 112, 2nd paragraph have been obviated by Applicant's amendments.

4. The rejections of claims 24-30, 32-33, 35-39, 41-42 and 44 under 35 USC 102(b) as being anticipated by WO 93/15220 have been withdrawn in response to Applicant's amendments to recite first and second reagent mixtures containing the specific ingredients noted. The rejections of claims 31, 34, 40, and 43 under 35 USC 103(a) as being unpatentable over WO 93/15220 have been withdrawn in response to the above amendments and upon further consideration by the Examiner. It is noted that although the previous Office action refers to WO 93/15220 as "Cockbain et al."; however, as the first inventor is actually Sundregagen et al., the WO 93/15220 publication will be referred to herein below as "Sundrehagen et al.".

Specification

5. The specification is objected to because required subject headings, e.g. the "BACKGROUND OF THE INVENTION," "BRIEF SUMMARY OF THE INVENTION," and the "BRIEF DESCRIPTION OF THE DRAWINGS" are absent.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Claim Objections

6. Claims 24, 26, 35-36, 38, 44, 45, 52-53, and 57 are objected to because of the following informalities:

7. Claim 24 is objected to because it is suggested that in the first instance of the abbreviation "SAH" in the claims that it be accompanied by the full term.

8. Claims 24 and 36 are objected to because the claims recite a "second enzyme" prior to mentioning the "first enzyme". Since the "first enzyme" is always SAH hydrolase throughout the claims, Applicant may wish to simply refer to this enzyme by its name only in order to avoid confusion.

9. Claims 26, 35, 38, 44, 45, 52-53, and 57 are objected to because they refer to "said" "**secondary**" antibody. However, the independent claims refer to a "second" antibody rather than a "secondary" antibody. Applicant is requested to employ consistent terminology throughout the claims.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 24-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New Matter

12. Claims 24-25 and 36-37 recite a "polyhapten having hapten moieties **comprising** S-adenosine homocysteine" (emphasis added). However, the specification only discloses polyhaptens where the hapten *is* SAH, and does not describe haptens that "comprise" SAH. Because of the "comprising" transitional language currently employed, the claims are drawn to a genus of polyhapten molecules where the hapten moieties *include* S-adenosine homocysteine (SAH). This language would include any additional moieties, structures, modifications, etc., to the hapten moieties so long as the SAH structure is present. The amendments therefore broaden the scope of the disclosure and claims as originally filed.

Written Description

13. Claims 24-25 and 36-37 recite a "primary antibody capable of binding to said polyhapten" and a "second antibody capable of binding to said complex". Claims 26, 35, 38, 44-45, 52-53 and 57 also refer to primary and/or secondary antibodies.

It is noted that the specification defines the term "**antibody**" in such a way so as to encompass "single chain antibodies, antibody fragments (e.g. Fab fragments), and oligopeptides and oligonucleotides" (page 5, the first full paragraph; see also page 10, the first full paragraph).

Thus, the claims are not limited to antibodies *per se* since the term "antibody" as it is employed in the claims would include not only antibodies but any fragments thereof, as well as non-antibody oligopeptides and oligonucleotides.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed. The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention." MPEP 2163.

The specification provides a description of primary antibodies that are specific for SAH and of secondary anti-mouse IgG antibodies, and outlines art-recognized techniques for producing such antibodies (see page 5). However, the specification does not provide a written description to support evidence of possession of the claimed genus of "primary antibodies" that are capable of binding to a polyhapten in light of Applicant's definition of "antibody". Likewise, the specification does not provide an adequate written description of "second antibodies" that are capable of binding to the polyhapten-primary antibody complex that is commensurate with the scope of the claims.

The specification fails to describe any non-antibody oligopeptides or oligonucleotides with any particularity. The specification does not disclose any partial structure or relevant identifying characteristics that would be shared by the members of the genus of "antibodies" that bind to SAH and/or polyhapten-antibody complex. There is no disclosed correlation between any partial structure (for example, a polynucleotide binding motif) and function (ability to bind to SAH and/or polyhapten-antibody complex). The specification does not describe any methods of making any non-antibody oligopeptide or oligonucleotide "antibodies" against a polyhapten or

polyhapten complex. The specification fails to disclose any partial structure, relevant identifying characteristics, or method of making specific ligands that are RNA, DNA or proteins other than antibodies.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus of "antibodies".

14. In addition, it is noted that Applicant's definition of "antibody" also encompasses a genus of "**antibody fragments**". However, the specification does not provide an adequate written description of the genus of antibody fragments for the following reasons. Such a genus would include (for example) fragments of an antibody that are as small as a single amino acid residue. Because of the large number of possible ways in which an antibody molecule could be fragmented into smaller portions, the claims are drawn to a large genus of molecules that cannot be readily envisaged based on its sheer size.

It is known that antibody molecules are made up of characteristic structural units defined by the presence of two heavy chains and two light chains (see Harlow, E. and Lane, D., Antibodies: A Laboratory Manual (1988) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, pages 7-13 and 23-26). Antibodies interact with their cognate antigens via their variable regions, which are formed by amino acids from both heavy and light chains (see especially pages 12 and 23-26).

In the instant case, the claims are drawn to methods of using any conceivable antibody fragment. In light of the teachings of Harlow & Lane, one skilled in the art would not envisage

possession of methods of using all antibody fragments to capture antigen, since only those fragments *that retain the antigen-binding variable regions* would be able to bind to antigen. For example, one skilled in the art could not envisage possession of an antibody fragment that consists of a single heavy chain, since such a fragment would not include an antigen-binding site since it is not enough to define a variable region.

Furthermore, the specification does not disclose any partial structure or other identifying characteristics that would be shared by the members of the genus of "antibody fragments" claimed. There is no disclosed correlation between a shared structure and function (ability to bind to antigen) among the members of the genus. Although the specification discloses the example of Fab fragments (page 5), the specification does not describe how to make all possible types of antibody fragments. In particular, the specification does not describe how to make any antibody fragments that lack the antigen-binding site, yet are still able to bind to polyhapten or polyhapten complex as claimed.

For all of these reasons, while the genus of (full-length) antibodies and Fab fragments thereof is adequately described, the specification does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of methods of using *all* antibody fragments as capture agents. Applicant is reminded that new matter should not be introduced into the specification.

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 24-35 and 45-52 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: **a step in which homocysteine is assayed**. The preambles of independent claims 24 and 25 recite a method "for assaying homocysteine in a sample". However, the body of the claims does not set forth any active steps in which homocysteine is actually detected. Rather, the claims conclude with the step of detecting a complex between a polyhapten and a primary antibody. The claims lack a method step that clearly relates back to the objective of the method (assaying homocysteine) as recited in the preamble.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 24-26, 29-30, 32-33, 36-39, 41-42, 45, 48, 49-51, and 53-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frantzen et al. ("Enzyme conversion immunoassay for determining total homocysteine in plasma or serum" *Clinical Chemistry* 44:2 (1998), 311-316) in view of Zuk et al. (4,208,479).

Frantzen et al. teach a competitive immunoassay method for determining homocysteine (Hcy) in plasma or serum substantially as claimed, in which a sample is contacted with the following reagents: adenosine, reducing agent (DTT), a "first enzyme" (SAH hydrolase or

SAHase), a "second enzyme" (adenosine deaminase or Adoase) capable of converting adenosine to inosine, polyhapten (BSA-S-adenosyl-L-homocysteine (SAH) conjugate), primary antibody capable of binding to polyhapten (mouse anti-SAH antibody), second antibody capable of binding to polyhapten-first antibody complex (anti-mouse antibody). See the entire document, in particular the abstract; p. 311-312, the sections "Materials and Methods" and "Assay Method"; and Figure 2. The reference further teaches photometrically detecting the complex by spectrophotometric reading (Figure 2).

Frantzen et al. further teach a blocking solution (see p. 312, "Coating of microtiter plates"), which would be considered to be an "agent which promotes precipitation" of the polyhapten-antibody complex in that the blocking agent would reduce nonspecific binding to the microtiter plates, and thus promote formation and precipitation of the specific complex. The reference also teaches heparin (see p. 313, left column, "Blood samples"), which is disclosed an example of an agent promoting precipitation (see the instant specification at page 6). The reference also teaches thimerosal, which is used as an inhibitor of SAHase in order to remove excess adenosine (p. 316, left column). This would also be considered to be an agent that promotes precipitation of the polyhapten-antibody complex since the reference discloses that the anti-SAH antibody can cross-react somewhat with adenosine (ibid), such that by removing excess adenosine the thimerosal would promote formation and precipitation of the antibody-polyhapten complex. Thus, given the broadest reasonable interpretation of an "agent which promotes precipitation", any of the above reagents would read on the claim limitation.

Frantzen et al. differs from the claimed invention in that although it teaches the same reagents claimed, it fails to specifically teach mixing the reagents together into two or three different reagent mixtures in the specific manner claimed.

Rather, the Frantzen et al. reference teaches mixing the sample with a reagent mixture of adenosine, reducing agent, and first enzyme, followed by addition of second enzyme (see Figure 2). This sample is then contacted with polyhapten (coated on a microtiter plate), followed by sequential addition of primary and second antibody (ibid and p. 312, "The enzyme assay" and "The immunoassay").

However, the prior art recognized the value of combining together multiple reagents needed for performing an assay into reagent mixtures. For example, Zuk et al. teach that reagents for performing an assay can be combined together in a kit for substantial convenience as well as enhancement in accuracy (column 22, lines 20-68). In particular, the reference teaches that *it is desirable to combine as many reagents as possible in a single vessel*, with certain provisos, for example that the reagents mixed must not adversely interact with each other, as would occur if enzymes and their substrates were mixed. The reagents can be provided in aqueous form as concentrated solutions or as dilute ready to use solutions. This allows for accurate transfer and a predetermined final concentration and ratio of reagents. Besides the reagents necessary for the assay, there will normally be other additives, e.g. various stabilizers and preservatives.

Therefore, in light of the prior art teachings of Zuk et al. (for example), it would have been obvious to one of ordinary skill in the art at the time of the invention to combine together the necessary reagents for performing the homocysteine assay of Frantzen et al. for the art-recognized benefits of convenience and improvement in assay accuracy. Keeping in mind the art-

recognized importance of ensuring that the reagents mixed together are stable and do not adversely interact with each other (i.e., enzymes and their substrates should not be provided together), as taught for example by Zuk et al., it would have been a matter of routine skill in the art to combine the reagents together in the particular manner(s) claimed, given the limited number of reagents and thus the limited number of possible ways in which the reagents may be combined together while providing SAHase separately from its substrate adenosine. The selection of any order of mixing ingredients is prima facie obvious (MPEP 2144.04).

With respect to claims 32, 41, and 55, Zuk et al. teach that besides reagents necessary for the assay, other additives are normally included, such as serum albumin, which acts as a stabilizer (column 22, lines 53-62). Therefore, it would have been obvious to include serum albumin as taught by Zuk et al. in the reagent mixture(s) of Frantzen et al. and Zuk et al. in order to stabilize the reagents. It is noted that albumin is disclosed in the specification as an example of a carrier protein according to the instant invention at page 7.

With respect to claims 33, 42, and 56, Frantzen et al. teach a backbone structure (BSA) onto which the SAH moieties are conjugated (p. 311, right column, the last paragraph).

19. Claims 24-30, 32-33, 36-39, 41-42, 45-51, and 53-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sundrehagen et al. (WO 93/15220) in view of Zuk.

Sundrehagen et al. teach methods and kits for assaying homocysteine in a sample (e.g. blood, plasma or urine), for example by competitive immunoassay, in which the test sample is contacted with adenosine and SAH hydrolase (see in particular the abstract; page 3, the last paragraph to page 9; and pages 23-25). As one example, a polyhapten can be provided that

competes with the analyte (homocysteine) for binding to a particle-bound antibody, which is then detected by turbidimetric or nephelometric measurement (page 14). The method employs the following reagents: a polyhapten, which can be SAH itself (p. 16-17), a "first enzyme" that is SAH hydrolase, a second enzyme capable of converting adenosine (adenosine deaminase or adenosine kinase), adenosine or an adenosine analog, a primary antibody capable of binding to the polyhapten (anti-SAH antibodies; see Example 7 and pages 16 and 34 in particular), a reducing agent (p. 7-8 and 15),

The reference further teaches photometric detection of antibody:polyhapten complexes, for example by turbidimetric or nephelometric measurement as noted above (see for example the paragraph bridging p. 3-4 and pages 14 and 24-25).

Sundrehagen et al. differs from the claimed invention in that although it teaches the same reagents claimed, it fails to specifically teach mixing the reagents together into two or three different reagent mixtures in the specific manner claimed. The reference also fails to specifically teach kits comprising stable *aqueous* mixtures of the reagents.

However, the prior art recognized the value of combining together multiple reagents needed for performing an assay into reagent mixtures. For example, Zuk et al. (discussed above) teach that reagents for performing an assay can be combined together in a kit for substantial convenience as well as enhancement in accuracy (column 22, lines 20-68). In particular, the reference teaches that *it is desirable to combine as many reagents as possible in a single vessel*, with certain provisos, for example that the reagents mixed must not adversely interact with each other, as would occur if enzymes and their substrates were mixed. The reagents can be provided in aqueous form as concentrated solutions or as dilute ready to use solutions. This allows for

accurate transfer and a predetermined final concentration and ratio of reagents. Besides the reagents necessary for the assay, there will normally be other additives, e.g. various stabilizers and preservatives.

Therefore, in light of the prior art teachings of Zuk et al. (for example), it would have been obvious to one of ordinary skill in the art at the time of the invention to combine together the necessary reagents for performing the homocysteine assay of Sundrehagen et al. for the art-recognized benefits of convenience and improvement in assay accuracy. Keeping in mind the art-recognized importance of ensuring that the reagents mixed together are stable and do not adversely interact with each other (i.e., enzymes and their substrates should not be provided together), as taught for example by Zuk et al., it would have been a matter of routine skill in the art to combine the reagents together in the particular manner(s) claimed, given the limited number of reagents and thus the limited number of possible ways in which the reagents may be combined together while providing SAHase separately from its substrate adenosine. It would have been further obvious to provide the reagent mixtures in aqueous form for the convenience of a ready-to-use format, as taught by Zuk et al. The selection of any order of mixing ingredients is prima facie obvious (MPEP 2144.04).

One would have a reasonable expectation of success because Sundrehagen et al. teach that the necessary reagents may be added to the reaction mixture either in a sequential manner or simultaneously (see page 23).

With respect to claims 26, 38, 45, and 53, Sundrehagen et al. also teach a secondary antibody (sheep anti-mouse IgG) that specifically binds to the primary antibody (which is a mouse IgG anti-SAH antibody) (see page 34).

With respect to claims 28 and 47, Sundrehagen et al. teach that detection may be performed either at the reaction end point or alternatively, either at one or more fixed time points or via kinetic measurement (page 22).

With respect to claims 32, 41, 50, and 55, Sundrehagen et al. teach that carrier proteins can be added as additives to enhance SAH hydrolase stability during storage or during the assay itself (see the paragraph bridging p. 15-16). Zuk et al. also teach that besides reagents necessary for the assay, other additives are normally included, such as serum albumin, which acts as a stabilizer (column 22, lines 53-62). Therefore, it would have been obvious to include serum albumin as taught by Zuk et al. in the reagent mixture(s) of Frantzen et al. and Zuk et al. in order to stabilize the reagents. It is noted that albumin is disclosed in the specification as an example of a carrier protein according to the instant invention at page 7.

With respect to claims 30, 39, 49, and 54, Sundrehagen et al. teach sucrose (see the paragraph bridging pages 15-16), which is a polysaccharide; polysaccharides are disclosed as examples of suitable agents according to the instant specification at page 6.

With respect to claims 33, 42, 51, and 56, Sundrehagen et al. teach conjugating the hapten to BSA or hemocyanin (page 16).

20. Claims 30-31 and 39-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frantzen et al. in view of Zuk et al., or alternatively over Sundrehagen et al. in view of Zuk et al. as applied to claims 24 and 36 above, and further in view of either Karl et al. (US 6,210,975) or Lin et al. (US 4,298,592, Applicant's IDS of 6/25/01).

Frantzen et al., Zuk et al., and Sundrehagen et al. are as discussed above, which fail to specifically teach polyethylene glycol as a component of one of the reagent mixtures.

Karl et al. teach immunoassay methods for the detection of analytes, in which polyethylene glycol is added to the reaction mixture in order to reduce error due to the hook effect (see especially the abstract and columns 1-2). Nephelometric and turbidimetric detection is also specifically taught (the abstract).

Lin et al. also teach providing polyethylene glycol having a molecular weight of from about 2,000 to about 10,000 in order to accelerate immunoprecipitation reactions (column 2, lines 36-68).

Therefore, it would have been obvious to include polyethylene glycol in the reagent mixtures of Frantzen et al. and Zuk et al. and/or Sundrehagen et al. and Zuk et al. in order to reduce sources of error due to the hook effect in an immunoassay as taught by Karl et al. and/or in order to accelerate the reaction as taught by Lin et al.

21. Claims 34 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frantzen et al. in view of Zuk et al., or alternatively over Sundrehagen et al. in view of Zuk et al. as applied to claims 33 and 42 above, and further in view of Yanaihara et al. (US 4,855,406).

The references are as discussed above. Sundrehagen et al. teach polyhaptens having a hapten such as SAH conjugated to BSA or hemocyanin (page 16). Frantzen et al. also teach the backbone structure BSA onto which the SAH moieties are conjugated (p. 311, right column, the last paragraph).

However, the references fail to specifically teach that the backbone structure is porcine thyroglobulin.

Yanaihara et al. teach carrier molecules to which haptens may be bound (column 7, lines 24-50). In particular, the reference teaches that both bovine serum albumin (as taught by Sundrehagen et al. and Frantzen et al.) as well as porcine thyroglobulin are known carriers to which haptens may be bound. The Courts have ruled that art-recognized equivalence between embodiments provides a strong case of obviousness in substituting one material for another. See MPEP 2144.06.

Because Yanaihara et al. teach that bovine serum albumin and porcine thyroglobulin are recognized as equivalents applied for the same purpose (binding to haptens), it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute porcine thryoglobulin, as taught by Yanaihara et al., for bovine serum albumin of Frantzen et al. or Sundrehagen et al. in the method and kit of Frantzen et al. and Zuk et al. or of Sundrehagen et al. and Zuk et al.

22. Claims 35, 44, 52, and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frantzen et al. in view of Zuk et al., or alternatively over Sundrehagen et al. in view of Zuk et al. as applied to claims 24-25 and 36-37 above, and further in view of either Hideo et al. (JP 04329357, Applicant's IDS of 6/25/01) or de Steenwinkel et al. (US 4,362,531).

The references are as discussed above, which fail to specifically teach a chaotropic salt.

However, Hideo et al. teach adding a chaotropic salt (urea, thiocyanate, or guanidine HCl) to a reaction mixture in order to reduce nonspecific binding in an immune nephelometric reaction (see the English abstract provided).

de Steenwinkel et al. also teach adding one or more chaotropic or chaotropic-like agents to a reaction mixture in order to reduce non-specific protein interaction interferences in particle agglutination immunoassays (see especially the abstract and columns 2-4 in particular). The chaotropic agents include chaotropic salts (column 3, lines 45-65).

Therefore, it would have been obvious to one of ordinary skill in the art to include chaotropic salts as taught by either Hideo et al. or de Steenwinkel et al. in the reaction mixtures of Frantzen et al. and Zuk et al., or alternatively of Sundrehagen et al. and Zuk et al. One would be motivated to do this in order to reduce nonspecific binding.

Response to Arguments

23. Applicant's arguments filed 11/14/06 have been fully considered but are moot in light of the new grounds of rejection set forth above.

Conclusion

24. Claims 24-57 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached at (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CFoster

Christine Foster, Ph.D.
Patent Examiner
Art Unit 1641

LONG V. LE 03/28/07
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600